

Circulating-tumor DNA analysis in patients with diffuse large B cell lymphoma

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Background/Aims: Circulating-tumor DNA in diffuse large B cell lymphoma There is ongoing interest whether circulating tumor DNA (ctDNA) from the blood plasma can serve as a minimal residual disease (MRD) which influencing decision making during the treatment of high-risk diffuse large B-cell lymphoma (DLBCL). In the current study, we collected blood samples sequentially before, and after the treatment from the patients with newly diagnosed DLBCL who received R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy, and we evaluated the possibility of clinical use of ctDNA as a biomarker (MRD) to determine up-front autologous stem cell transplantation (auto-SCT) after first-line chemotherapy for high-risk patients in practice.

Methods: Patients with pathologically confirmed DLBCL, patients scheduled to receive R-CHOP chemotherapy, and patients without restrictions on the proceeding the auto-SCT were enrolled. Blood samples were collected serially from the time of diagnosis, and after completing chemotherapy. To conduct ctDNA genotyping and ctDNA monitoring simultaneously, targeted sequencing by cancer personalized profiling by deep sequencing (CAPP-seq) was used. Then we compared changes in ctDNA before and after treatment to identify clinical roles.

Results: We could collect serum samples from 10 patients at the time of diagnosis (Table). In the analysis of ctDNA, majority genetic abnormality was missense mutation. In the current data, number of ctDNA mutations at the time of diagnosis were not significantly associated with risk group. In terms of tumor burden, changes in ctDNA mutation numbers did not correlate with changes of PET scan images, and treatment response. However, new mutations appeared after completing chemotherapy in patients with relapsed/refractory disease. PIK3CA, BRAF, TGM7, and EZH2 mutations were identified in the post-treatment samples which were not identified in the pre-treatment analysis (Figure).

Conclusions: Changes in ctDNA mutations before and after treatment can help determine the direction of treatment. In particular, autologous transplantation can be considered if a mutation indicating poor prognosis is newly discovered after treatment.

